Article

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Prevalence of depression and anxiety in patients with cystic fibrosis and parent caregivers: Results of The International Depression Epidemiological Study (TIDES) across Nine Countries

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Summary

Background: Individuals with chronic diseases and parent caregivers are at increased risk for symptoms of depression and anxiety. Prevalence of psychological symptoms was evaluated in adolescents and adults with cystic fibrosis (CF) and parent caregivers across nine countries. Predictors of symptomatology, comorbidity of psychological distress, and concordance between parents and adolescents were analyzed.

Methods: Patients with CF, ages 12 and older, and caregivers of children with CF, birth to18, completed measures of depression and anxiety measures across 154 CF Centers in Europe and the US. Psychological symptoms were compared across countries using X^2. Logistic regression examined extent of comorbid symptoms, predictors of depression and anxiety, and concordance between parent and adolescent symptomatology.

Findings: Psychological symptoms were reported by 6,088 patients with CF and 4,102 parents. Elevated symptoms of depression were found in 10% of adolescents, 19% of adults, 37% of mothers, and 31% of fathers. Elevations in anxiety were found in 22% of adolescents, 32% of adults, 48% of mothers and 36% of fathers. Overall, elevations were 2-3 times the rates in community samples. Analyses of comorbid symptoms indicated that adolescents reporting depression were 14·97 times more likely to report anxiety; adults elevated on depression were 13·64 times more likely to report anxiety; mothers with elevated depression were 15·52 times more likely to report anxiety; fathers with elevated depression were 9·20 times more likely to report elevated anxiety. Significant differences were found by patient age (depression: adolescents 19% vs. adults 29%; anxiety: adolescents 22% vs adults 32%). Mothers reported more symptoms of depression and anxiety than fathers, respectively (depression 37% vs. 31%; anxiety 48% vs. 36%). Predictors were identified: 1) patients (female, older, lower FEV_1 and BMI, on IVs, listed for transplant, hemoptysis/pneumothorax, psychiatric medications or psychotherapy; 2) parents (younger child, on IVs, psychiatric medications or psychotherapy). Concordance between 1122 parent-teen dyads indicated that adolescents were 2·32 and 2·22 times more likely to be elevated on depression and anxiety, respectively, if a parent was elevated.

Interpretations: Symptoms of depression and anxiety were elevated in both patients with CF and parents across several European countries and the US. Health variables were significantly related to psychological symptoms. Annual screening of psychological symptoms is recommended for both patients and parents.

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Introduction

Meta-analyses and systematic reviews have indicated that children and adults with chronic diseases, as well as parent caregivers, are at increased risk for depression and anxiety.[1,2,3] Cystic fibrosis (CF) is the most common genetic, life-limiting chronic disease among Caucasian populations and requires a treatment regimen that takes between two and four hours per day.[4] Patients have genetic mutations that affect the CF transmembrane conductance regulator protein, leading to thick mucus secretions, repeated infections and progressive failure of most organ systems (e.g., lungs, pancreas, and digestive, reproductive).[5] Although recent advances in diagnosis and treatment have led to increases in lifespan, CF continues to be one of the most difficult chronic conditions to manage.[6]

Studies evaluating depression and anxiety in patients with CF have generally found a high prevalence of psychological distress. Rates of depression in children and adolescents have ranged from 9-29%, using different methods of assessment (ICD-9 diagnoses, CDI).[7,8] For adults with CF, rates of depression have ranged from 13-30%[9,10] and rates of anxiety from 30% to 33%.[9,11] Among parent caregivers, elevations in psychological distress have also been found, with depression ranging from 20-35%.[7,12,13] Overall, psychological symptoms appear to be higher in this population than community samples;[14] however, these studies have been limited by small sample sizes and different screening or diagnostic tools, which have made interpretation of the results difficult. In addition, the majority of studies have only assessed symptoms of depression but not anxiety.

Psychological distress in patients with CF has been associated with a number of negative consequences and health outcomes, including worse adherence,[7,15] worse pulmonary function,[11,16] increased hospitalizations and health care costs,[17] and decreased health-related quality of life.[9,10] A recent study[17] compared adolescents with CF who had been diagnosed with a depressive disorder to a matched sample of non-depressed teens with CF, and found that those who were depressed were three times more likely to be hospitalized for a pulmonary exacerbation and incurred much higher health care costs over two years ($280,000 for the depressed group vs. $60,116 for the non-depressed group). Given both the wide range of prevalence estimates for patients with CF and their caregivers, and the negative impact these symptoms have on disease management and functioning, the TIDES (The International Depression Epidemiological Study) international study group aimed to screen depression and anxiety in several European countries and the United States. Two screening measures were utilized to assess these symptoms in both adolescents and adults with CF and parent caregivers. Predictors of psychological symptoms, both demographic and medical, were also identified.

Methods

Procedure

This study was conducted at 154 CF centers in nine countries: Belgium, Germany, Italy, Spain, Sweden, The Netherlands, Turkey, United Kingdom, and the United States. Screening was initiated in patients aged 12 through adulthood and in parents of children birth to 18 years of age. Study protocols were approved by national and local ethics committees or institutional review boards at all CF centers.

Staff members approached participants at routine, stable clinic visits. After completion of consent/assent, patients or parents completed a basic demographic questionnaire in addition to the screening measures. When both parents were present, they completed the symptom measures independently. Depression and anxiety screening measures were scored immediately by trained staff members to identify clinically elevated scores; referrals were provided if necessary. Completion of the measures took approximately 15 minutes. Medical data were collected through chart review.

Participants

Across nine countries, 1286 adolescents (*M* age = 14·84, *SD* = 1·69) and 4739 adults (*M* age = 28·87, *SD* 9·5) with CF were screened. Inclusion criteria were: 1) confirmed diagnosis of CF, 2) age within specified range, and 3) screening during stable clinic visit. Patients who had received a solid organ transplant were excluded. In addition, 3127 mothers and 975 fathers of younger children reported on their own symptoms. Descriptive demographic and medical data are presented in Table 1.

Measures

Demographic and medical characteristics. Parents and young adults completed a Background Information Form assessing parent and child/adolescent's age, gender, and education. Information about pharmacological and psychological treatment of depression and anxiety was also collected. Indicators of physical health status in the past *six months* were recorded from medical charts (FEV_1% predicted, height, weight, hemoptysis/pneumothorax, IV antibiotics, and listed for transplant).

Hospital Anxiety and Depression Scale.[18] The HADS is a 14-item instrument; seven questions measure depression and seven measure anxiety. It has extensive reliability and validity data, and was designed specifically for patients with chronic medical conditions (i.e., removal of somatic items). Respondents indicated the severity of each symptom on a 4-point rating-scale (0-3) over the past week. Maximum score is 21; participants were categorized using established cutoff scores (mild = 8-10, moderate =11-15, severe = $\geq$16). Validated translations were used in Europe.

Center for Epidemiological Studies-Depression Scale.[19] The CES-D is a well-established self-report measure of depressive symptomatology for community samples. It has 20 items measuring symptoms of depression that reflect diagnostic criteria on the DSM-IV and has correlated well with diagnostic interviews. Items are rated on a 4-point scale from 0 to 3, with higher scores indicating more depressive symptoms. The maximum score is 60, with $\geq$ 16 = elevated. Valid translations were used in Europe.

Statistical Analyses

Statistical analyses. Demographic and prevalence estimates were stratified by country to test for differences. Prevalence estimates were based on published cut-scores[18,19] and divided into two groups according to "caseness:" 1) non-case (below cut-off) and 2) case (mild-severe

symptoms). Effect sizes were calculated to assess variability across strata: Cramér's V(φ_c) for categorical and eta-square (η^2) for continuous variables. Logistic regression identified comorbid symptoms within individuals and predictors of elevated symptoms. Regression analyses were pooled across countries, with country of origin as a categorical covariate to account for the nesting of participants within countries. Missing data occurred because countries did not collect data for a particular question or participants did not provide a response. Amount of missing data was small, ranging from 0% to 7% depending on the measure. Separate analyses were run for each characteristic. Concordance between 1130 parent-adolescent dyads was evaluated with logistic regression. All analyses were run using SAS 9·3.

Role of the funding source. The funding sources had no involvement in the in study design; collection, analysis, and interpretation of data; in the writing of the report; and in the decision to submit the paper for publication. The corresponding author confirms she had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Demographics. Demographic and health information for patients and caregivers are presented in Table 1 and reported by country in Table 2. On average, patients were in their mid-20's, about half were female, BMI was in the normal range, and lung function indicated moderate disease severity. Significant variability was found across countries on age, gender, BMI, and FEV_1% predicted, however these effects were small. Across countries, hemoptysis/pneumothorax (2-32%), currently on IV antibiotics (5-19%), listed for transplant (2-12%), and pharmacological/psychological treatment of depression or anxiety (3-23%).

Prevalence of Symptoms of Depression. Rates of depression varied depending on age and the screening tool: adolescents 5-19%, adults 13-29%, mothers 20-34%, and fathers 18-25% (Table 1 and Figure 1). Analyses by country indicated that overall, 11% of patients were elevated on the HADS-D (range 8-15%) and 27% of patients were elevated on the CES-D (range 20%-31%) (Table 2). Because the sample size for Turkey was small and the availability of standard medications for CF is limited, their estimates were not included in the ranges above (i.e., depression on the HADS-D=29%, CES-D=52%). Statistically significant differences were found by age (see Table 1), with adolescents reporting fewer symptoms of depression than adults (19% vs. 29% on the CES-D; $p<.001$). Mothers reported significantly more depressive symptoms than fathers on the CES-D (34% vs. 25%; $p<.001$), but not on the HADS-D (20% vs. 18%).

For the countries that administered both the HADS-D and CES-D to patients, significant differences in prevalence rates were found between measures. Adolescents were 5·32 ($p <·01$) and adults were 2·24 ($p <·01$) times more likely to report elevated symptoms of depression on the CES-D than the HADS-D. For parents, mothers were 2·15 ($p <·01$), and fathers 1·57 ($p <·01$) times more likely to report elevations on the CES-D than the HADS-D.

Prevalence of Symptoms of Anxiety. Symptoms of anxiety were prevalent in patients and parents: adolescents 22%, adults 32%, mothers 48%, and fathers 36% (see Table 1 and Figure 1). Analyses by country indicated high rates of anxiety among patients (mean 30%), with moderate variability across countries (14%-35%; Turkey falls within this range). Statistically significant

differences were found by age, with 22% of adolescents vs. 32% of adults (p<·001) reporting elevations in anxiety above the cutoff score (see Table 1, Figure 1). Mothers also reported significantly more symptoms of anxiety than fathers (48% vs. 36%, p<·001).

Comorbidity between depression and anxiety. Adolescents reporting depression were 14·97 times more likely to also report anxiety, with 6% reporting elevations in both. For adults the odds ratio was 13·64, with 14% reporting both depression and anxiety. Mothers reporting depression were 15·52 times more like to also report anxiety, with 31% reporting both and for fathers the odds ratio was 9.20, with 21% reporting both depression and anxiety. All effect sizes were large.

Predictors of depression and anxiety. Logistic regressions indicated that, for adolescents, the following characteristics were associated with elevated symptoms of depression on the CES-D or HADS-D: being female (Odds Ratio [OR] = 1·77), an episode of hemoptysis/ pneumothorax in past six months (OR= 3·82), taking psychiatric medication for depression or anxiety (OR = 3·96), and receiving psychotherapy for depression or anxiety (OR = 6·54; Table 3). Characteristics associated with elevated anxiety were: being female (OR = 1·63), episode of hemoptysis/pneumothorax in past six months (OR=2·03), recently on IV antibiotics (OR = 1·73), taking psychiatric medications (OR=1·91), and receiving psychotherapy (OR=2·77).

For adults, depression was associated with: older age (OR=1·02 per year), lower FEV_1% predicted (OR=0·90 per 10% change), hemoptysis or pneumothorax in past six months (OR=1·62), recently on IV antibiotics (OR=1·65), listed for transplant (OR=1·39), taking psychiatric medications (OR=3·56), and receiving psychotherapy (OR=3·21). Characteristics associated with elevated symptoms of anxiety were: older age (OR=1·02 per year), being female (OR=1·66), lower BMI (OR=1·03 per unit), lower FEV_1 (OR =0·96 per 10% change), hemoptysis/pneumothorax (OR=1·38), listed for transplant (OR=1·34), taking psychiatric medications (OR=3·37), and receiving psychotherapy (OR=4·22).

For mothers, child characteristics associated with depression were: recently on IV antibiotics (OR=1·53) and receiving psychotherapy (OR=1·88). Elevated anxiety was associated with: younger age (OR= 1·03 per year), recent IV antibiotics (OR=1·52), and receiving psychotherapy (OR=2·02). For fathers, only one child medical variable was associated with depression: recent IV antibiotics (OR=1·72).

Concordance between parent and adolescent depression and anxiety. For the 1122 dyads with both parent and teen report, adolescents were 2·39 times more likely be above the cut-off for depression if at least one of their parents had elevated symptoms and they were 2·22 times more likely to be above the cut-off for anxiety if their parent was also elevated.

Discussion

This is the largest psychological screening study to date conducted in a rare disease, with data collected from both European countries and the US. Results across nine countries revealed high rates of depression and anxiety in adolescents and adults with CF, as well as parent caregivers. Elevated depression was reported by 17% of patients across countries, regardless of which screening tool was used—a rate two times that reported in community populations (9·2%).[20]

Similarly, although there are fewer large-scale studies of caregivers, 37% of mothers and 31% of fathers reported clinically elevated depression, which is three times the rate in community samples.[20,21] Rates of anxiety were also elevated in patients and caregivers, with 30% of patients and 36-48% of parents above the clinical cut-off. These rates are approximately twice those reported in the community.[22]

Given these high rates of psychological symptoms and their documented effects on disease management, including clinic attendance and adherence to prescribed treatments,[23] annual screening of depression and anxiety for adolescents and adults with CF and parent caregivers is warranted. This conclusion is consistent with several international guidelines, which recommend regular screening for adolescents and adults with chronic conditions—particularly if these symptoms impact daily functioning and management of the disease.[24–28] For example, the American Diabetes Association recommends screening of psychological symptoms at "regular clinical encounters" and when there is "concern about poor management"[28] To date, however, there is no guideline recommendation for screening parent caregivers.

As found in prior studies, comorbidity of depressive and anxious symptoms within individuals was high, suggesting that elevations in depression confer a heightened risk of elevations in anxiety. Analyses of parent-adolescent dyads showed that depression or anxiety in either parent doubled the risk that the adolescent would report elevated psychological distress. In addition to parents' reporting elevated symptoms in this large study, co-occurrence of symptomatology provides a second rationale for screening parent caregivers. Identification and treatment of parental psychological distress may both prevent adolescents with CF from developing psychological symptoms and when detected in parents, prompt the medical team to provide referrals for mental health services to the family.

We utilized two well-established screening measures of depression, and in countries that used both, comparisons indicated that the HADS-D under-estimated symptoms of depression by a factor of two. Recent studies comparing the HADS-D and PHQ-9 for the purposes of large-scale screening concluded there were significant psychometric problems with the HADS, including lack of sensitivity and a three, rather than two-factor structure.[20,29] A comparison of items on the HADS-D and CES-D revealed that many of the diagnostic criteria in the DSM-IV/5 were not represented on the HADS-D (e.g., cognitive impairment, lack of energy). Instead, the vast majority of items on the HADS-D measured anhedonia (72%), whereas the CES-D included items representing the full spectrum of depressive symptoms underlying this construct.

Several risk factors were associated with elevated depression and anxiety. Older age and female sex, worse disease severity, as indicated by lower lung function or BMI ,and recent *changes in health status* (past six months), such as hemoptysis or prescription of IV antibiotics. Treatments for psychological distress (with medication or psychotherapy) were the highest risk factors. For parents, recent course of IV antibiotics, and current treatment for a psychological disorder were associated with greater symptomatology.

Limitations and Future Directions

Although the demographic and health information from the three largest samples in this study (UK, US and Germany) appeared quite similar to data in their respective national registries,[12,16] it

is possible that this sample is not representative of the larger international population. In screening studies, those who are experiencing the most severe symptoms are less likely to attend regular clinic visits or give informed consent for participation in research, and thus, these prevalence rates may be an *underestimate* of the population.[30] This study was also limited by the cross-sectional nature of the data collection. Prospective, longitudinal studies are needed to determine: which health variables *predict* increases in psychological symptoms and what health *consequences* follow identification of elevated scores (e.g., decreased adherence, increases in pulmonary exacerbations, increases in healthcare utilization and cost, decreases in health-related quality of life).

These results highlight the importance of measuring and treating mental health issues in patients and families coping with serious, chronic illnesses. Our findings, in conjunction with other smaller studies, have led to the formation of an international committee, sponsored by both the European Cystic Fibrosis Society and the Cystic Fibrosis Foundation, to develop guidelines on mental health screening and treatment in CF. As advocated by other national guidelines committees, we have recommended annual screening of depression and anxiety in adolescents and adults with CF and parent caregivers.[25–28] Our goal is to implement these screening recommendations, utilizing the unique structure of accredited and recognized CF centers in Europe and the US, to promote their implementation.

Contributors

ALQ - was lead author, grant-holder, and manager of the database, data collection, data analysis and interpretation, and writing of the article.
LG- participated in planning the study, was responsible PI and grant-holder of the German part of the study, and participated in data interpretation and writing of the article.
JA and AD- participated in planning the study, was responsible PI and grant-holder of the UK part of the study, and participated in data interpretation and writing of the article.
PL - was responsible for obtaining the funding in Belgium, overseeing the data collection and entry, assisting with analysis of the data and interpretation of the results, and writing the manuscript.
AS - was responsible for the coordination and data collection of the Spanish part of the study and participated in the interpretation and writing of the article
MT - was responsible for the coordination and data collection of the Dutch part of the study and participated in the interpretation and writing of the article
AB - was responsible for collecting and entering the data for Sweden, interpreting the results, and writing the manuscript.
HY - was responsible for collecting and entering the data for Turkey, interpreting the results and writing the manuscript.
PC - was responsible for collecting and entering the data, interpreting the results of the Italian part of the study, and writing the manuscript.
LB - responsible for creating the database, cleaning the data, assisting with data analyses and interpretation and writing the manuscript.
DB - responsible for planning the study, developing the database, cleaning the data, assisting with the analyses and interpretation, and writing the manuscript.

Declaration of Interest

Dr. Quittner reports grants from Cystic Fibrosis Foundation during the conduct of the study. Dr. Goldbeck reports grants from Mukoviszidose Institut gGmbH during the conduct of the study. Dr. Abbott reports grants from UK CF Trust (Grant No. PJ544) during the conduct of the study. Dr. Duff reports grants from UK CF Trust (Grant No. PJ544) during the conduct of the study. Dr. Lambrecht reports grants from Belgian CF Foundation during the conduct of the study. Dr. Solé reports grants from Spanish Cystic Fibrosis Federation (FEFQ) during the conduct of the study. Dr. Tibosch reports grants from Dutch Cystic Fibrosis Organization (NCFS), during the conduct of the study. Dr. Bergsten Brucefors has nothing to disclose. Dr. Yuksel has nothing to disclose. Dr. Catastini reports grants from CF Italian Foundation, during the conduct of the study. Dr. Blackwell has nothing to disclose. Dr. Barker has nothing to disclose.

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Table 1· Participant Characteristics by Respondent

	Respondent							
	Adolescent	**Adult**	**Effect Size**	**P-Value**	**Mothers[a]**	**Fathers[a]**	**Effect Size**	**P-Value**
Sample size	1286	4739			3127	975		
Age, mean (SD), years	14·84 (1·69)	28·87 (9·54)	·31	<·01	8·90 (5·08)	8·52 (5·14)	<·01	·04
Female	669 (53%)	2271 (48%)	·03	<·01	1558 (50%)	460 (47%)	·03	·08
BMI, mean (SD)	19·54 (3·11)	21·87 (3·54)	·07	<·01	17·47 (2·99)	17·28 (2·92)	<·01	·10
FEV_1 percent predicted, mean (SD)	83·78 (23·44)	62·32 (24·51)	·12	<·01	89·23 (21·55)	90·74 (22·13)	<·01	·12
Hemoptysis or pneumothorax in six months	35 (3%)	657 (14%)	·14	<·01	37 (1%)	9 (1%)	<·01	·84
Currently on IV antibiotics	156 (12%)	733 (16%)	·03	·04	299 (10%)	118 (12%)	·04	·02
Listed for transplant	7 (1%)	243 (5%)	·09	<·01	12 (0·4%)	1 (0·1%)	·02	·23
Currently on psychiatric medication for dep/anx	44 (4%)	466 (10%)	·09	<·01	59 (2%)	9 (0·9%)	·03	·11
Currently receiving psychotherapy for dep/anx	70 (6%)	379 (8%)	·03	·03	103 (3%)	19 (2%)	·02	·23
Positive Scores					Caregivers			
HADS-D	60 (5%)	609 (13%)	·11	<·001	618 (20%)	173 (18%)	·02	·16
CES-D	87 (19%)	488 (29%)	·09	<·001	1057 (34%)	240 (25%)	·08	<·001
Either HADS-D or CES-D	130 (10%)	913 (19%)	·10	<·001	1165 (37%)	305 (31%)	·05	<·001
HADS-A	281 (22%)	1503 (32%)	·09	<·001	1496 (48%)	343 (36%)	·11	<·001

Notes: [a] Characteristics of younger patients whose parents completed the screening

Table 2· Participant characteristics by country.

	Countries											
	BE	**DE**	**IT**	**NL**	**ES**	**SE**	**TR**	**UK**	**US**	**Total**	**Effect Size**	***p*-value**
Sample size	426	663	741	515	275	167	52	2042	1207	6088		
Age, mean (SD), years	25·55 (10·09)	23·53 (9·22)	24·52 (9·38)	27·50 (11·39)	25·82 (7·81)	26·84 (12·16)	12·86 (5·97)	26·98 (10·18)	25·40 (10·86)	25·76 (10·31)	·03	<·001
Female	201 (47)	316 (48)	383 (52)	239 (47)	119 (43)	81 (49)	32 (63)	993 (49)	527 (53)	2963 (49)	·06	·01
BMI, mean (SD)	20·58 (3·34)	19·93 (2·98)	20·52 (3·05)	21·33 (3·15)	21·36 (3·82)	21·84 (3·33)	18·71 (3·99)	22·10 (3·78)	21·70 (3·83)	21·34 (3·60)	·05	<·001
FEV_1 percent predicted, mean (SD)	72·34 (24·55)	67·22 (25·60)	73·83 (26·97)	66·25 (26·12)	64·67 (26·12)	74·66 (26·89)	71·90 (26·26)	62·55 (24·49)	67·89 (26·08)	66·99 (25·84)	·03	<·001
Hemoptysis/pneumothorax last six months	31 (7)	27 (4)	--	101 (24)	32 (12)	4 (4)	1 (2)	279 (14)	223 (32)	698 (14)	·17	<·001
Currently on IV antibiotics	72 (17)	--	--	56 (11)	14 (5)	19 (19)	8 (18)	129 (6)	182 (17)	461 (11)	·16	<·001
Received an organ transplant	10 (2)	18 (3)	--	27 (6)	20 (7)	2 (2)	1 (2)	43 (2)	131 (12)	252 (5)	·18	<·001
Currently on psychiatric medication for dep/anx	40 (9)	14 (2)	--	16 (3)	17 (6)	8 (5)	3 (7)	158 (8)	257 (23)	513 (10)	·24	<·001
Currently receiving psychotherapy for dep/anx	22 (5)	53 (9)	--	17 (3)	13 (5)	11 (12)	3 (7)	145 (7)	190 (18)	401 (9)	·17	<·001
HADS Depression											·08	<·001
Non-Case (0-7)	361 (85)	599 (90)	638 (86)	466 (90)	244 (89)	154 (92)	37 (71)	1810 (89)	1052 (91)	5361 (89)		
Case (8-21)	65 (15)	63 (10)	103 (14)	49 (10)	31 (11)	13 (8)	15 (29)	232 (11)	100 (9)	671 (11)		
CES-D Depression	106 (28)	--	--	102 (20)	75 (31)	--	16 (52)	--	259 (29)	558 (27)	·11	<·001
Either HADS or CES-D	122 (29)	63 (10)	103 (14)	114 (22)	83 (30)	13 (8)	30 (58)	232 (11)	287 (25)	1047 (17)	·11	<·001
HADS Anxiety											·14	<·001
Non-Case (0-7)	286 (67)	526 (79)	486 (66)	443 (86)	204 (74)	129 (77)	36 (69)	1374 (67)	755 (66)	4239 (70)		
Case (8-21)	140 (33)	136 (21)	255 (34)	72 (14)	71 (26)	38 (23)	16 (31)	668 (34)	397 (35)	1793 (30)		

Notes: unless otherwise noted, values represent No. (%), only participants with non-missing values were included in the calculation of the percentages· BE: Belgium, DE: Germany, IT: Italy, NL: Netherlands, ES: Spain, SE: Sweden, TR: Turkey, UK: United Kingdom, US: United States; "--" indicates data was not collected.

Table 3· Univariate logistic regression results

		Respondent							
		Adolescent		Adult		Mother		Father	
		Odds Ratio (95% CI)	*p* - value	Odds Ratio (95% CI)	*p* - value	Odds Ratio (95% CI)	*p* - value	Odds Ratio (95% CI)	*p* - value
HADS or CESD Depression	Age, years	1·01 (0·89-1·13)	0·96	1·03 (1·02-1·04)	**<·01	0·99 (0·98-1·01)	·32	0·99 (0·96-1·01)	·30
	Female	1·77 (1·17-2·66)	*0·01	1·09 (0·94-1·26)	·28	0·95 (0·81-1·10)	·47	0·93 (0·70-1·23)	·61
	BMI	1·03 (0·98-1·10)	0·26	1·01 (0·99-1·03)	·27	1·01 (0·98-1·03)	·70	1·03 (0·99-1·09)	·17
	FEV_1 percent predicted [a]	0·98 (0·90-1·06)	0·62	0·90 (0·88-0·93)	**<·01	1·00 (0·96-1·04)	·97	0·95 (0·88-1·03)	·20
	Hemoptysis/pneumothorax in last six months	3·82 (1·63-8·95)	**<·01	1·62 (1·33-1·98)	**<·01	0·96 (0·47-1·97)	·92	1·29 (0·31-5·34)	·72
	IV antibiotics*	1·74 (0·94-3·21)	0·08	1·65 (1·33-2·04)	**<·01	1·53 (1·17-2·01)	**<·01	1·72 (1·12-2·63)	*·01
	Received an organ transplant [b]	--	--	1·39 (1·03-1·87)	*·03	1·10 (0·31-3·85)	·88	--	--
	Currently on psychiatric medication for dep/anx	3·96 (1·94-8·08)	**<·01	3·56 (2·86-4·42)	**<·01	1·51 (0·88-2·61)	·14	0·68 (0·14-3·33)	·63
	Currently receiving psychotherapy for dep/anx	6·54 (3·56-12·01)	**<·01	3·21 (2·54-4·06)	**<·01	1·88 (1·25-2·83)	**<·01	0·52 (0·15-1·84)	·31
HADS Anxiety	Age, years	0·99 (0·91-1·07)	·79	1·02 (1·01-1·03)	**<·01	0·98 (0·97-1·00)	*·03	0·98 (0·95-1·00)	·08
	Female	1·63 (1·23-2·15)	**<·01	1·66 (1·46-1·88)	**<·01	0·94 (0·81-1·09)	·40	0·83 (0·63-1·09)	·17
	BMI	0·99 (0·95-1·04)	·79	1·03 (1·01-1·05)	**<·01	0·99 (0·97-1·02)	·50	0·98 (0·94-1·03)	·53
	FEV_1 percent predicted [a]	1·01 (0·95-1·07)	·76	0·96 (0·93-0·98)	**<·01	0·99 (0·95-1·03)	·54	0·99 (0·91-1·06)	·71
	Hemoptysis/pneumothorax in last six months	2·03 (0·99-4·14)	*·05	1·38 (1·15-1·65)	**<·01	1·32 (0·67-2·58)	·42	0·82 (0·20-3·44)	·79
	IV antibiotics*	1·73 (1·13-2·66)	*·01	1·14 (0·94-1·37)	·18	1·52 (1·16-1·98)	**<·01	1·10 (0·71-1·71)	·67
	Received an organ transplant [b]	--	--	1·34 (1·01-1·77)	*·04	0·91 (0·29-2·90)	·88	--	--
	Currently on psychiatric medication for dep/anx	1·91 (1·00-3·68)	*·05	3·37 (2·74-4·14)	**<·01	0·97 (0·57-1·65)	·92	0·64 (0·16-2·63)	·54
	Currently receiving psychotherapy for dep/anx	2·77 (1·65-4·62)	**<·01	4·22 (3·37-5·30)	**<·01	2·02 (1·32-3·09)	**<·01	2·03 (0·79-5·17)	·14

Notes: [a] Odds ratios are for a 10% change in FEV_1 percent predicted. [b] Variable was not included in the model for 12-18 year olds due to small number of cases.

Figure 1· Rates of depression and anxiety by respondent